temperature. After removal of the foil, the room lights being off, the ampule was broken open and the absorbance recorded. Absorbances were read to three decimal places with use of a Perkin-Elmer Lambda 3 spectrophotometer. The infinity readings were obtained by placing a foil-wrapped ampule of each set in a steam bath for at least 1 h before recording the absorbance.

B. For compounds obtained in small amounts, a variation on the above procedure was used. A solution with the appropriate concentration of the *trans*-azobenzene in isooctane was prepared, and about 3 mL was sealed in a 1-cm^2 quartz ampule. This ampule was irradiated in the RUL photoreactor in a water-cooled immersion well for at least 3 h. The constant-temperature bath described above was used to heat the cuvette holder of the spectrophotometer. The ampule was partially preheated in the reservoir of the constant-temperature bath before being placed into the heated cuvette holder. It was then left for 30–60 s to establish temperature equilibrium, and a zero time and absorbance were recorded. Between readings, a black-felt-covered card was placed in the light beams to prevent any photochemical isomerization. The infinity reading was obtained by placing the ampule in a steam bath in the dark for at least 1 h, putting it back in the spectrophotometer, waiting for temperature equilibration with the card in place, and finally recording the absorbance. The temperature was determined by using a similar unsealed ampule placed in the heated cuvette holder after the kinetic run was completed (usually while waiting for the infinity reading). This ampule was filled with isooctane to the same height as the sealed ampules. An electronic (thermistor) thermometer with a flexible cable was used to read the temperature.

Variable Temperature. C. Solutions and ampules were prepared as in method A and irradiated. The thermal isomerization was carried out by using a thermostated oil bath whose heater was controlled with a variable autotransformer. The temperature was measured with an electronic (thermistor) thermometer, the probe of which was placed in an ampule of isooctane similar to the test ampules. At suitable temperature intervals, one or more tubes were removed from the thermostat and cooled quickly in an ice bath. The corresponding temperature and time were recorded, and the absorbance was measured after the ampule was allowed to return to room temperature. The infinity readings were obtained by leaving one or more ampules in a steam bath for at least 1 h before recording their absorbances.

Data Analysis. Activation energies were calculated from the raw kinetic observations of absorbance, temperature, and time by a one-step procedure, full details of which will be published elsewhere. Briefly, the computational method consists of substituting the Arrhenius equation directly into the first-order rate expression (Abs, Abs_0, and Abs_{inf} are absorbances at time t, time 0, and the infinity reading).

Thus,

$$\int_0^t \frac{d(Abs - Abs_{inf})}{Abs - Abs_{inf}} = -\int_0^t k\, dt = -\int_0^t Ae^{-E_a/RT}\, dt \quad (1)$$

For a constant-temperature kinetic run, integration affords eq 2, while when the temperature varies, eq 1 must be integrated

$$Abs - Abs_{inf} = (Abs_0 - Abs_{inf}) \exp(-At \exp(-E_a/RT)) \quad (2)$$

numerically. In either case, an iterative procedure allows trial values of A and E_a to be fitted to the known values of Abs, Abs_0, time (t), and temperature (T).

Acknowledgment. This work was supported financially by the Natural Sciences and Engineering Research Council of Canada through operating grants to N.J.B. and G.F., and through a postgraduate scholarship to C.L.F. We thank Dr. H. Rau for supplying us with samples of compounds 10 and 11, Dr. L. R. C. Barclay for a gift of compound 12, and the Ethyl Corp. for gifts of ortho-alkylated anilines.

Supplementary Material Available: Final atomic coordinates, details of molecular geometry, and thermal parameters (9 pages). Order information is given on any current masthead page. A structure factor listing is available from G.F. (28 pages). Tables of all raw kinetic data are available from N.J.B. (18 pages).

Retinoids. 6.[1] Preparation of Alkyl- and Trimethylsilyl-Substituted Retinoids via Conjugate Addition of Cuprates to Acetylenic Esters[†]

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Received July 1, 1986

Five retinoids bearing the ethyl, *tert*-butyl, and trimethylsilyl groups in the 9-position of retinal and the ethyl and *tert*-butyl groups in the 13-position have been synthesized. The key step of the syntheses involves the conjugate addition of lithium diethylcuprate, lithium di-*tert*-butylcuprate, and lithium bis(trimethylsilyl)cuprate, respectively, to the acetylenic esters 4 and 13. The stereoselectivity of this reaction was examined in detail; it proceeds stereoselectively cis in THF at −78 °C. Various isomers of the newly prepared retinoids were isolated by preparative HPLC and characterized by the usual spectroscopic methods. The dependence of the configuration and conformation of the polyene chain on the introduced group was studied by means of NMR and UV spectroscopy.

Introduction

Retinal (1) plays a pivotal role in two light energy converting processes, (i) the process of vision in vertebrates[2] and (ii) the proton pumping process in *Halobacterium halobium*;[3] the proteins responsible for these processes, rhodopsin and bacteriorhodopsin, respectively, both contain retinal as the prosthetic group[2,4] (Figure 1).

[†] Dedicated to Professor Dr. S. Hünig on the occasion of his 65th birthday.

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mercially available β-ionone (2). The preparation of the acetylenic hydrocarbon 3 has been reported by Negishi et al.[15] and proceeds via enolization of 2, formation of the enol phosphate, and phosphate elimination; this reaction is particularly valuable since it represents the reversal of the well-known hydration of terminal acetylenes to methyl ketones. Metalation of 3 and reaction of the resulting lithium acetylide with methyl chloroformate according to a general procedure of Brandsma[16] furnished ester 4 in 71% yield. With this compound in hand the addition of lithium diethylcuprate was investigated in detail; the results obtained are as follows.

(i) Lithium diethylcuprate is usually prepared by addition of 2 equiv of ethyllithium[17] to 1 equiv of copper(I) iodide in diethyl ether or THF at 0 °C.[18,19] In order to achieve complete consumption of 4 it proved useful to employ up to 50% excess of lithium diethylcuprate with respect to 4; this does not give rise to side reactions.

(ii) After addition of 4 in diethyl ether or THF solution to lithium diethylcuprate, the reaction is complete within 1 h at −78 °C or within 5 min at 0 °C. Subsequent quenching with methanol or water, extractive workup, and purification provides ester 5a in more than 80% yield (cf. Experimental Section).

(iii) The sole reaction of the cuprate with 4 is the conjugate addition; no regioisomers are formed.

(iv) The stereoselectivity of the addition reaction may be controlled by means of the solvent and the reaction temperature as summarized in Table I.

In THF at −78 °C the addition proceeds stereoselectively cis; at higher temperatures, in diethyl ether or upon quenching with water instead of methanol this selectivity is lost, presumably because of increasing isomerization of the double bond in the enolate formed before quenching.[13] These results are in good agreement with those obtained by Corey et al.[13] for the addition of lithium dialkylcuprates to methyl 2-decynoate and methyl 2-butynoate. For the synthesis of 19-nor-9-ethylretinal (10a) this stereoselectivity was not required since we intended to prepare the 9-cis and 9-trans isomers of 10a in one sequence and to separate them by preparative HPLC.

The subsequent steps leading to 10a are standard procedures in vitamin A chemistry and were carried out without difficulties. Reduction of ester 5a with $LiAlH_4$[20] (81%) and reoxidation with activated manganese dioxide[21] (53%) furnished aldehyde 7a, which was converted to 19-nor-9-ethylretinonitrile (9a) by Wittig–Horner olefination with the anion of the C_5-phosphonate 8[22] (89%). Reduction of 9a with DIBAH[23] eventually provided the target molecule 10a in 55% yield; the overall yield of 10a from 4 is 17.7% (5 steps). The product mixture consisted of the four expected isomers 9-*cis*-, 9-*cis*,13-*cis*-, 13-*cis*, and *all-trans*-10a. The separation of the isomers by preparative HPLC proved to be difficult, and 9-*cis*, 13-*cis*- and 13-*cis*-10a could no be obtained in analytically pure form. Nevertheless it was possible to collect the ^1H and ^{13}C NMR data of all four isomers using 2D $^{13}C,^1H$ correlation spectroscopy (see paragraph at the end of the paper about supplementary material).

The synthesis of 19-nor-9-*tert*-butylretinal (10b) proceeded as described for 10a; however, some differences should be emphasized. Lithium di-*tert*-butylcuprate is known to be thermally more labile than lithium diethylcuprate.[19] It is therefore prepared by addition of 2 equiv of commercially available *tert*-butyllithium solution in pentane to 1 equiv of copper(I) iodide in THF at −30 °C. After addition of 4, stirring at −20 °C for 2 h is required to effect complete consumption of 4; the conditions sufficient for the addition of lithium diethylcuprate (−78 °C, 1 h) provided only partial consumption of 4. The resultant ester 5b, obtained in 87% yield, consisted out of the 9-cis (9*E*) isomer exclusively, although the reaction conditions are rather vigorous compared with the preparation of 5a. These findings are explained by the bulkiness of the *tert*-butyl group; in fact, it is remarkable that the *tert*-butyl group can be introduced into the 9-position of retinal since this position is sterically shielded by the methyl groups of the cyclohexene ring.

The subsequent steps proceeded without difficulty and afforded 19-nor-9-*tert*-butylretinal (10b) in 36.2% overall yield from 4 (5 steps). The product mixture consisted of 9-*cis*- and 9-*cis*,13-*cis*-10b, respectively; thus no isomerization of the 9,10 double bond has occurred on the way from 5b to 10b. This fact again illustrates the great steric demand of the 9-*tert*-butyl group.

A considerable extension of the methodology described for the introduction of alkyl groups could be achieved by the use of lithium bis(trimethylsilyl)cuprate for the conjugate addition to 4. Silyl cuprates like $(PhMe_2Si)CuLi$[24] and $(Me_3Si)_2CuLi$[24,26] have been introduced into preparative organic chemistry by Fleming, who essentially examined the following reactions of these cuprates: (i) conjugate addition to α,β-unsaturated carbonyl compounds, in particular esters, (ii) conjugate displacement of tertiary allylic acetates, and (iii) addition to nonactivated terminal acetylenes.[24,25] Lithium bis(trimethylsilyl)cuprate, however, has found only little application since the trimethylsilyllithium required is not readily available; it is made either by treatment of bis(trimethylsilyl)mercury[26] with lithium[27] or by reaction of hexamethyldisilane with methyllithium.[28] We chose the latter method for the preparation of (trimethylsilyl)lithium, which by treatment with copper(I) iodide provided the desired cuprate.[25] The optimum conditions for the addition to 4 turned out to be a 15% excess of the cuprate, a temperature of −30 °C, and a reaction time of 2 h. Under these conditions the substrate was consumed completely; the product, however, contained not only the desired α,β-unsaturated ester 5c, but also the product formed by a second addition of the cuprate to 5c. This observation is not surprising since silyl cuprates are known to undergo conjugate addition reactions to α,β-unsaturated esters;[24,25] carbon cuprates show this reaction only in rare cases.[29]

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Table II. UV Data of Retinal[32] and the Retinoids Prepared in This Work

	λ_{max}, nm (ϵ)			
	all-trans	9-cis	13-cis	9-cis,13-cis
1[a]	383 (42 884)	373 (36 010)	375 (35 500)	368 (32 380)
10a[b]	387 (38 200)	380 (33 900)		
10b[b]		354 (25 900)		350 (24 500)
10c[b]		373 (21 700)		365 (18 400)
15a[b]			382 (27 600)	382 (23 100)
15b[b]			[c]	[c]

[a] In ethanol. [b] In dichloromethane. [c] The UV spectra exhibit no distinct absorption maxima: 13-*cis*-15b: λ_{max} (ϵ) 230 (13 700), 253 (13 100), 337 (16 300), 364 nm (15 500). 9-*cis*,13-*cis*-15b: λ_{max} (ϵ) 232 (14 000, shoulder), 252 (15 900), 290 (13 800), 322 (13 000), 333 (12 200, shoulder), 357 nm (9800, shoulder).

butyl resonance in 9-*cis*-10b was saturated, enhancements were observed of the 7-H, 8-H, and 10-H signals. This proves the 9-cis configuration and shows that more than one conformer with respect to the C(8)–C(9) single bond is involved (see Figure 2). Chemical shift comparison then led to the configuration of the C(9)–C(10) double bond in 9-*cis*,13-*cis*-10b.

A similar result was obtained for the trimethylsilyl derivative 10c. Saturation of the trimethylsilyl signal in 9-*cis*-10c caused strong enhancements of the 7-H and 10-H resonances and a weak enhancement of the 8-H resonance; this result proves the 9-cis configuration and reveals the presence of both 8-s-cis and 8-s-trans conformers, the latter being more highly populated than in the *tert*-butyl analogue (see Figure 2). By chemical shift comparison the second isomer of 10c was shown to have the 9-cis,13-cis configuration. In a similar way, the configurations of the C(13)–C(14) double bonds in both isomers of 15b were shown to be cis. Saturation of the 13-*tert*-butyl resonance in 13-cis-15b gave enhancements of the 12-H and 14-H signals; saturation of the aldehyde proton resonance enhanced the 11-H and 14-H signals. Besides proving the 13-cis configuration, these experiments indicate a preference for the 12-s-cis (or a closely related gauche) conformation (see Figure 2).

Conformational control of polyenes by the *tert*-butyl and similar bulky groups is not a new finding; a particularly well-known example is 2-*tert*-butyl-1,3-butadiene. The first hint for the preference of a s-cis conformation in this molecule was its high reactivity in Diels–Alder reactions[34] and in the addition of SO_2;[35] direct proof for the presence of this conformation was received from several spectroscopic investigations.[36-38]

An impression of the influence of the newly introduced group on the polyene chain can also be obtained by comparison of the ^1H and ^{13}C NMR chemical shifts of the retinoids with those of retinal.[32] As expected, the values for the ethyl analogues are similar to those of retinal except in the immediate vicinity of the ethyl substituent, whereas the *tert*-butyl and the trimethylsilyl group influence greater parts of the molecule.

Similar conclusions can be drawn from the comparison of the UV data of the newly prepared retinoids with those of retinal (see Table II).

Again, the retinoids bearing the ethyl substituent in the 9- or 13-position, respectively, behave similarly to retinal; in contrast the 9-*tert*-butyl derivative 10b exhibits a hypsochromic shift of 20–30 nm with a concomitant decrease of the extinction coefficient. It is obvious that the bulky *tert*-butyl group diminishes the degree of conjugation in the retinal molecule, probably by repulsive interactions with the adjacent hydrogen atoms of the polyene chain and subsequent distortion of the molecule. In the case of the 9-trimethylsilyl analogue 10c this effect is weaker, presumably due to the electropositivity of the Me_3Si group and its greater distance from the polyene chain. Finally, the isomers of 20-nor-13-*tert*-butylretinal (15b) show a completely different behavior; the spectra have no similarity with those of retinal. Instead of the strong long-wave band (α-band) of retinal, they possess several bands at shorter wavelengths (β-bands), a behavior that is known from several isomers of retinal with a preference of a twisted 12-s-cis conformation.[39] Hence, this observation confirms the result of the NOE experiments.

Conclusion

The addition of cuprates to the readily accessible acetylenic esters 4 and 13 represents a novel, flexible way to retinoids bearing alkyl and silyl groups in the 9- and 13-position, respectively; in the present work five retinoids have been synthesized by this method. The reaction proceeds even with bulky groups like the *tert*-butyl and the trimethylsilyl groups; the only exception is the introduction of the Me_3Si group into the 13-position of retinal, which could not be achieved. In principle, this approach should be applicable to all alkyl and silyl groups, provided that the corresponding lithium compound can be prepared and that the group is not too bulky to be inserted into the molecule.

The newly synthesized retinoids possess several interesting features, the most intriguing one being the influence of the introduced group on the configuration and conformation of the polyene chain. In the ethyl analogues the adjacent doubld bond of the polyene chain can exist in the cis or trans configuration; the conformation resembles that of retinal. In the *tert*-butyl and trimethylsilyl retinoids, on the other hand, the adjacent double bond is forced into the cis configuration; furthermore the s-cis conformation of the neighboring single bond is increasingly favored in the series 9-Me_3Si < 9-*tert*-butyl < 13-*tert*-butyl. Thus the introduction of voluminous groups represents a way to control the configuration and conformation of the polyene chain and to make retinoids to measure.

Experimental Section

Materials. Diethyl ester and THF were distilled from $LiAlH_4$. β-Ionone was distilled under vacuum. All other reagents were of analytical grade and were used without further purification.

Analyses. ^1H NMR spectra were recorded on a Varian T-60 (CCl_4), a Bruker AM 300 ($CDCl_3$), or a Bruker WM 400 spectrometer ($CDCl_3$) with $(CH_3)_4Si$ as the internal standard. ^{13}C NMR spectra were obtained on a Bruker AM 300 or a Bruker WM 400 spectrometer with $CDCl_3$ as the solvent and the internal standard (δ 77.05). The ^{13}C NMR spectra of 9-cis-10b and of all isomers of 10a, 10c, 15a, and 15b were assigned by two-dimen-

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^{13}C NMR δ 168.2 (s, 11-C), 163.4 (s, 9-C), 137.6 (s, 6-C), 133.5 (s, 7-C), 129.7 (s, 5-C), 126.8 (d, 8-C), 112.7 (d, 10-C), 51.0 (q, 11-OCH_3), 39.6 (t, 2-C), 37.0 (s, 9-CCH_3), 34.2 (s, 1-C), 33.0 (t, 4-C), 29.5 (q, 9-CCH_3), 28.8 (q, 1-CH_3), 21.4 (q, 5-CH_3), 19.2 (t, 3-C); UV (ethanol) λ_{max} (ϵ) 211 nm (9300); MS, m/e 290 (M^+); exact mass calcd for $C_{19}H_{30}O_2$ 290.2246, found 290.2245.

3-*tert*-Butyl-5-(2,6,6-trimethylcyclohexen-1-yl)-2,4-pentadien-1-ol (6b). The reduction of 3.78 g (13 mmol) of 5b in 20 mL of diethyl ether with a suspension of 0.57 g (15 mmol) of $LiAlH_4$ in 15 mL of diethyl ether was carried out as described for 6a. After kugelrohr distillation (130 °C/0.005 mbar), 2.97 g of 6b (11.3 mmol, 87%) was obtained as a colorless, viscous oil: IR (CCl_4) ν 3620, 3600–3200 cm^{-1}; ^{1}H NMR (300 MHz) δ 5.86 (d, 1 H, 8-H, $J_{7,8}$ = 16.2 Hz), 5.81 (d, 1 H, 7-H), 5.55 (t, 1 H, 10-H, $J_{10,11}$ = 6.4 Hz), 4.34 (d, 2 H, 11-H), 2.01 (m, 2 H, 4-H), 1.74 (s, 3 H, 5-CH_3), 1.64–1.58 (m, 2 H, 3-H), 1.48–1.45 (m, 2 H, 2-H), 1.10 (s, 9 H, 9-CCH_3), 1.02 (s, 6 H, 1-CH_3); ^{13}C NMR δ 151.0 (s, 9-C), 137.9 (s, 6-C), 132.8 (d, 7-C), 129.7 (d, 8-C), 128.8 (s, 5-C), 122.0 (d, 10-C), 61.2 (t, 11-C), 39.6 (t, 2-C), 35.8 (s, 9-CCh_3), 34.1 (s, 1-C), 32.9 (t, 4-C), 29.7 (q, 9-CCH_3), 28.9 (q, 1-CH_3), 21.8 (q, 5-CH_3), 19.3 (t, 3-C); UV (ethanol) λ_{max} (ϵ) 211 (6300), 247 nm (6900); MS, m/e 262 (M^+); exact mass calcd for $C_{18}H_{30}O$ 262.2297, found 262.2297.

3-*tert*-Butyl-5-(2,6,6-trimethylcyclohexen-1-yl)-2,4-pentadienal (7b). The oxidation of 2.78 g (10.6 mmol) of 6b in 200 mL of diethyl ether with 34.8 g (0.4 mol) of activated manganese dioxide was carried out as described for 7a and yielded 1.98 g of 7b (7.6 mmol, 72%, yellow oil) after purification by column chromatography: IR (CCl_4) ν 1670 cm^{-1}; ^{1}H NMR (300 MHz) δ 9.83 (d, 1 H, 11-H, $J_{10,11}$ = 7.4 Hz), 6.19 (d, 1 H, 7-H, $J_{7,8}$ = 15.6 Hz), 6.13 (d, 1 H, 8-H), 6.09 (d, 1 H, 10-H), 2.05 (m, 2 H, 4-H), 1.77 (s, 3 H, 5-CH_3), 1.65–1.61 (m, 2 H, 3-H), 1.50–1.46 (m, 2 H, 2-H), 1.17 (s, 9 H, 9-CCH_3), 1.04 (s, 6 H, 1-CH_3); ^{13}C NMR δ 193.6 (d, 11-C), 172.7 (s, 9-C), 139.1 (d, 7-C), 137.3 (s, 6-C), 131.5 (s, 5-C), 127.7 (d, 8-C), 125.9 (d, 10-C), 39.5 (t, 2-C), 36.8 (s, 9-CCH_3), 34.0 (s, 1-C), 33.0 (t, 4-C), 29.2 (q, 9-CCH_3), 28.9 (q, 1-CH_3), 21.8 (q, 5-CH_3), 19.1 (t, 3-C); UV (ethanol) λ_{max} (ϵ) 240 (9950), 294 nm (6300); MS, m/e 260 (M^+); exact mass calcd for $C_{18}H_{28}O$ 260.2140, found 260.2141.

19-Nor-9-*tert*-butylretinonitrile (9b). The Wittig–Horner reaction of 1.30 g (5 mmol) of 7b in 5 mL of diethyl ether, 2.17 g (10 mmol) of phosphonate 8[22] in 10 mL of THF and 0.4 g of sodium hydride (10 mmol, 60% in mineral oil) in 10 mL of THF was carried out as in the case of 9a. After column chromatography 1.54 g of 9b (4.8 mmol, 95%) was obtained as a yellow oil: IR (CCl_4) ν 2210 cm^{-1}; ^{1}H NMR (60 MHz) δ 7.1–6.0 (m, 3 H, 10-H, 11-H, 12-H), 5.95 (m, 2 H, 7-H, 8-H), 5.2–5.0 (m, 1 H, 14-H), 2.2–2.0 (m, 2 H, 4-H), 2.12 (s, 3 H, 13-CH_3), 1.78 (s, 3 H, 5-CH_3), 1.7–1.5 (m, 4 H, 2-H, 3-H), 1.15 (s, 9 H, 9-CCH_3), 1.07 (s, 6H, 1-CH_3); MS, m/e 323 (M^+); exact mass calcd for $C_{23}H_{33}N$ 323.2613, found 323.2615.

19-Nor-9-*tert*-butylretinal (10b). Aldehyde 10b was obtained by reduction of 647 mg (2 mmol) of 9b in 10 mL of hexane with 4.0 mL of DIBAH (4.0 mmol, 1.0 M solution in hexane) as described for 10a. Purification of the crude product by column chromatography furnished 460 mg of 10b (1.41 mmol, 70%) as a yellow oil. Product composition by HPLC analysis: 10% 9-*cis*,13-*cis*- and 90% 9-*cis*-10b. IR (CCl_4, 9-*cis*-10b): ν 1665 cm^{-1}. ^{1}H and ^{13}C NMR: see paragraph at the end of the paper about supplementary material. UV: see Table II. MS: m/e 326 (M^+); exact mass calcd for $C_{23}H_{34}O$ 326.2610, found 326.2609.

5-(2,6,6-Trimethylcyclohexen-1-yl)-3-(trimethylsilyl)-2,4-pentadienal (7c). To a solution of 2.27 g (15.5 mmol) of hexamethyldisilane in 8 mL of HMPTA was added 9.4 mL of MeLi (15.0 mmol, 1.6 M solution in diethyl ether) at 0 °C; the resulting red solution was stirred at this temperature for 15 min and treated with 30 mL of THF and 1.43 g (7.5 mmol) of copper(I) iodide. After another 20 min at 0 °C, the suspension was cooled to −30 °C and 1.50 g (6.5 mmol) of 4 in 15 mL of THF was added dropwise. The suspension was stirred at −30 °C for 2 h and quenched with 5 mL of methanol. Addition of water was followed by extractive workup, furnishing 1.96 g of crude ester 5c as a red oil. The ester was dissolved in 20 mL of diethyl ether and added to a suspension of 285 mg (7.5 mmol) of $LiAlH_4$ in 20 mL of diethyl ether at −65 °C. The suspension was stirred for 2 h at −30 °C and hydrolyzed with 5 mL of saturated NH_4Cl solution. The precipitate formed was filtered off and washed with diethyl ether; drying of the filtrate and evaporation of the solvent yielded 1.72 g of crude alcohol 6c. Oxidation to 7c was accomplished by stirring a solution of 6c in 50 mL of diethyl ether with 8.7 g (0.1 mol) of activated manganese dioxide for 17 h. After filtration, evaporation of the solvent, and column chromatography 480 mg of aldehyde 7c (1.7 mmol, 27% from 4) was obtained as a yellow oil: IR (CCl_4) ν 1670 cm^{-1}; ^{1}H NMR (400 MHz) δ 10.06 (d, 1 H, 11-H, $J_{10,11}$ = 7.8 Hz), 6.70 (d, 1 H, 8-H, $J_{7,8}$ = 15.9 Hz), 6.32 (d, 1 H, 7-H), 6.16 (d, 1 H, 10-H), 2.01 (m, 2 H, 4-H), 1.72 (s, 3 H, 5-CH_3), 1.63–1.56 (m, 2 H, 3-H), 1.48–1.42 (m, 2 H, 2-H), 1.01 (s, 6 H, 1-CH_3), 0.22 (s, 9 H, 9-$SiCH_3$); ^{13}C NMR δ 191.1 (d, 11-C), 164.5 (s, 9-C), 137.7 (s, 6-C), 137.2 (d, 7-C), 135.8 (d, 10-C), 131.7 (s, 5-C), 130.0 (d, 8-C), 39.5 (t, 2-C), 34.2 (s, 1-C), 33.1 (t, 4-C), 29.0 (q, 1-CH_3), 21.9 (q, 5-CH_3), 19.2 (t, 3-C), −1.2 (q, 9-$SiCH_3$); UV (ethanol) λ_{max} (ϵ) 211 (7900), 236 (8100), 323 nm (6000); MS, m/e 276 (M^+); exact mass calcd for $C_{17}H_{28}OSi$ 276.1909, found 276.1909.

19-Nor-9-(trimethylsilyl)retinonitrile (9c). The reaction of 80 mg of sodium hydride (2.0 mmol, 60% in mineral oil) in 2 mL of THF, 434 mg (2.0 mmol) of 8[22] in 2 mL of THF, and 223 mg (0.81 mmol) of 7c in 1 mL of diethyl ether was carried out as described for 9a and yielded after column chromatography 150 mg of 9c (0.44 mmol, 55%, yellow oil): IR (CCl_4) ν 2210 cm^{-1}; ^{1}H NMR (60 MHz) δ 7.3–5.9 (m, 5 H, 7-H, 8-H, 10-H, 11-H, 12-H), 5.2–5.1 (m, 1 H, 14-H), 2.2–2.0 (m, 2 H, 4-H), 2.15 (s, 3 H, 13-CH_3), 1.73 (s, 3 H, 5-CH_3), 1.7–1.5 (m, 4 H, 2-H, 3-H), 1.05 (s, 6 H, 1-CH_3), 0.22 (s, 9 H, 9-$SiCH_3$); MS, m/e 339 (M^+); exact mass calcd for $C_{22}H_{33}NSi$ 339.2382, found 339.2382.

19-Nor-9-(trimethylsilyl)retinal (10c). As described for 10a, the reduction of 136 mg (0.4 mmol) of 9c in 1 mL of hexane with 0.8 mL of DIBAH (0.8 mmol, 1.0 M solution in hexane) provided 75 mg of 10c (0.22 mmol, 55%, red oil) after purification by column chromatography. The mixture of isomers was analyzed by HPLC and consisted of 16% 9-*cis*,13-*cis*- and 84% 9-*cis*-10c. IR (CCl_4, 9-*cis*-10c): ν 1670 cm^{-1}. ^{1}H and ^{13}C NMR: see the paragraph at the end of the paper about supplementary material. UV: see Table II. MS: m/e 342 (M^+); exact mass calcd for $C_{22}H_{3}$ 342.2379, found 342.2410.

3-Methyl-1-(2,6,6-trimethylcyclohexen-1-yl)-1,3,5-octatrien-7-yne (12). To a solution of 38 mmol of lithium diisopropylamide (from 3.85 g diisopropylamine in 60 mL of THF and 23.8 mL of 1.6 M *n*-butyllithium in hexane) was added 9.30 g (38 mmol) of crude β-C_{18}-ketone 11[31] in 20 mL of THF at −78 °C. The mixture was stirred at −78 °C for 1 h, and 6.56 g (38 mmol) of diethyl chlorophosphate was added. The mixture was allowed to warm to room temperature and was added to a solution of 80 mmol of lithium diisopropylamide (from 8.10 g of diisopropylamine in 120 mL of THF and 50.0 mL of 1.6 M *n*-butyllithium in hexane) at −78 °C. The mixture was warmed to room temperature within 1 h and stirred for another 2 h. Water (80 mL) was added, and the major part of the solvent was removed by rotatory evaporation. The mixture was extracted with diethyl ether; the organic layers were washed with 1 N hydrochloric acid and water and dried. Evaporation of the solvent was followed by column chromatography providing 3.66 g of 12 (15.2 mmol, 42%) as a red oil: IR (CCl_4) ν 3310, 2100 cm^{-1}; ^{1}H NMR (60 MHz) δ 7.1–5.4 (m, 5 H, 7-H, 8-H, 10-H, 11-H, 12-H), 2.95 (d, 1 H, 14-H, $J_{12,14}$ = 2 Hz), 2.2–2.0 (m, 2 H, 4-H), 1.97 (s, 3 H, 9-CH_3), 1.70 (s, 3 H, 5-CH_3), 1.7–1.5 (m, 4 H, 2-H, 3-H), 1.03 (s, 6 H, 1-CH_3); MS, m/e 240 (M^+); exact mass calcd for $C_{18}H_{24}$ 240.1878, found 240.1880.

Methyl 20-Nor-13,14-didehydroretinoate (13). The reaction of 0.60 g (2.5 mmol) of 12 in 2 mL of diethyl ether with 1.5 mL of *n*-butyllithium (2.5 mmol, 1.7 M solution in hexane) and 0.33 g (3.5 mmol) of methyl chloroformate was carried out as described for the ester 4, yielding 407 mg of 13 (1.36 mmol, 55%, red oil) after purification by column chromatography: IR (CCl_4) ν 2210, 1715 cm^{-1}; ^{1}H NMR (60 MHz) δ 7.3–5.4 (m, 5 H, 7-H, 8-H, 10-H, 11-H, 12-H), 3.72 (s, 3 H, 15-OCH_3), 2.2–2.0 (m, 2 H, 4-H), 2.00 (s, 3 H, 9-CH_3), 1.7–1.5 (m, 4 H, 2-H, 3-H), 1.68 (s, 3 H, 5-CH_3), 1.02 (s, 6 H, 1-CH_3); MS, m/e 298 (M^+); exact mass calcd for $C_{20}H_{26}O_2$ 298.1933, found 298.1931.

Methyl 20-Nor-13-ethylretinoate (14a). A suspension of 500 mg (2.6 mmol) of copper(I) iodide in 4 mL of THF was treated with 4.2 mL of ethyllithium (5.2 mmol, 1.25 M solution in diethyl ether[17]) at 0 °C. A solution of 522 mg (1.75 mmol) of 13 in 4 mL

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